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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/554,567	09/01/00	AGUZZI	A 6458.US.01

EXAMINER	
ROARK, J	
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Offic Action Summary	Application No. 09/554,567	Applicant(s) AGUZZI ET AL.	
	Examiner Jessica H. Roark	Art Unit 1644	

-- The MAILING DATE of this communication app ars on the cover sheet with the correspondenc address --

Period f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 March 2000 and 29 June 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's amendments, filed 3/21/00 and 6/29/01 (Paper Nos. 5 and 8), are acknowledged.
Claims 1-28 have been canceled.
Claims 32-34 have been added.
Claims 29-34 *are pending.*

2. Applicant's election of Group XII in Paper No. 8 is acknowledged. The Examiner confirms the placement of claims 32-34 in elected Group XII. However, Applicant's cancellation of claims 1-28 has rendered moot the previous restriction requirement.

Claims 29-34 *are under consideration in the instant application.*

3. Sequence compliance: The instant application appears to be in sequence compliance for patent applications containing nucleotide sequence and/or amino acid sequence disclosures.

4. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows: An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application in the first sentence of the specification (37 CFR 1.78). *Applicant should amend the first line of the specification to indicate priority is claimed under 35 U.S.C. 371 to PCT/EP98/08271.*

5. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

6. The documents cited in the international search report in a PCT national stage application have been considered; however applicant is invited to provide an Information Disclosure Statement to make such documents of record in the instant application. There is no requirement that the examiner list the documents on a PTO - 892 form. See 37 CFR 1.98.

7. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

8. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed.*

9. Formal drawings have been submitted which fail to comply with 37 CFR 1.84.
Please see the enclosed form PTO-948.

10. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

11. 35 U.S.C. § 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

12. Claims 29-31 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd. App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

For examination purposes, "Use" claims are prosecuted as "methods of use".

Such claims are also indefinite. See section 14A.

13. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 29-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 29-31 provide for the use of a ligand according to claim 28, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

B) Claims 29-31 are indefinite in that they either directly (claim 29) or indirectly (claims 30-31) depend on a cancelled claim. Claim 29 should be written as an independent claim.

C) Claims 29-34 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: step(s) which result in the "test"; e.g., what reagents are used, which assay system (bioassay, western, IHC, etc.).

D) Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 32-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Kuroda et al. (Infection and Immunity 1983; 41:154-61, see entire document).

Kuroda et al. teach that fractionated B cells and T cells obtained from the spleens of mice infected with the causative agent of Creutzfeldt-Jakob disease (CJD), a form of transmissible spongiform encephalopathy (TSE), can be injected into susceptible mice and transmit disease (see entire document, especially Tables 2 and 4).

Thus Kuroda et al. teach a method to test for the presence of transmissible spongiform encephalopathy comprising

obtaining a sample of spleen,
collecting B cells and collecting T cells from the sample,
and testing the B cells and/or T cells for the presence of transmissible spongiform encephalopathy.

The ability to transmit disease to another animal is a well established means of testing for the presence of an infectious agent. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties in the method taught by Kuroda et al.

17. Claims 32-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Manuelidis et al. (Science 1978; 200:1069-1071, see entire document).

Manuelidis et al. teach that maximal infectivity for Creutzfeldt-Jakob disease (CJD), a form of transmissible spongiform encephalopathy (TSE), resides in the buffy coat of whole blood, which contains the white blood cells (see entire document, especially the last full paragraph on page 1070).

Since the white blood cells of the buffy coat of whole blood are inherently B cells and T cells, Manuelidis et al. teach a method to test for the presence of transmissible spongiform encephalopathy comprising

obtaining a sample of whole blood (which is a heterogeneous mixture of cell types and other components),
collecting B cells and collecting T cells from the sample by isolating the buffy coat,
and testing the B cells and T cells contained within the buffy coat for the presence of transmissible spongiform encephalopathy.

Manuelidis et al. attribute their ability to demonstrate the infectivity of blood to an increase in the sensitivity of the assay made possible by collecting a specific fraction of whole blood (that inherently containing the B cells and T cells) (see entire document, especially the last full paragraph on page 1070).

The ability to transmit disease to another animal is a well established means of testing for the presence of an infectious agent. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties in the method taught by Manuelidis et al.

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

19. Claims 29-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over
O'Rourke et al (US Pat No. 6,165,784),
and/or Korth et al. (Nature 6 November 1997; 390:74-77),
in view of
Kuroda et al. (Infection and Immunity 1983; 41:154-61)
and/or Manuelidis et al. (Science 1978; 200:1069-1071).

The claims are broadly drawn to methods to test for the presence of transmissible spongiform encephalopathy (TSE) in B cells and/or T cells.

O'Rourke et al. teach methods to test for transmissible spongiform encephalopathy in lymphoid tissue using an antibody that serves as a ligand in various immunoassays, including immunohistochemistry, western immunoblots, and dot blots (see entire document, e.g., "Summary of the Invention"). O'Rourke et al. teach that antibody ligands may be either polyclonal sera or monoclonal antibodies (see entire document, e.g., column 5, especially lines 40-50). O'Rourke et al. also teach the importance of developing tests that allow non-invasive preclinical evaluation of animals suspected of being infected with TSE, versus the standard approach of assaying brain biopsy material (see entire document, including the "Background of the Invention", especially the summary statement at column 3, lines 27-31).

Korth et al. teach a method of detecting transmissible spongiform encephalopathy based upon a monoclonal antibody that is specific for the prion form of PrP (the causative agent in TSEs) versus the cellular form of PrP (see entire document, e.g. Abstract). Korth et al. teach that this antibody can be used to identify the prion form of PrP directly, thus providing a basis for a TSE test in living humans or animals, by lowering the detection threshold needed (see especially paragraph preceding "Methods" on page 77).

Neither O'Rourke et al. or Korth et al. teach collecting B cells and/or T cells from a test sample and directly testing these cell types for the presence of transmissible spongiform encephalopathy.

Kuroda et al. have been discussed supra and teach that fractionated B cells and T cells obtained from the spleens of mice infected with the causative agent of Creutzfeldt-Jakob disease (CJD), a form of TSE, can be injected into susceptible mice and transmit disease (see entire document, especially Tables 2 and 4).

Manuelidis et al. have also been discussed supra and teach that maximal infectivity for Creutzfeldt-Jakob disease (CJD), a form of transmissible spongiform encephalopathy (TSE), resides in the buffy coat of whole blood, which contains the white blood cells (see entire document, especially the last full paragraph on page 1070). Manuelidis et al. attribute their ability to demonstrate the infectivity of blood to an increase in the sensitivity of the assay made possible by collecting a specific fraction of whole blood (that now known to containing the B cells and T cells) (see entire document, especially the last full paragraph on page 1070).

Thus Kuroda et al. teach that both B cells and T cells can transmit TSE, and Manuelidis et al. teach that it is important to focus on these cellular populations to increase the sensitivity of assays for TSE infectivity. Both O'Rourke et al. and Korth et al. teach that sensitive tests for TSEs are provided by antibody-based assays. And O'Rourke et al. further point out that sampling and testing samples containing lymphocytes is a relatively non-invasive to the animal to be tested. Thus one of ordinary skill in the art at the time the invention was made would have found it obvious to improve the sensitivity of the TSE tests by collecting samples containing B cells and/or T cells and testing for the presence of TSE by using an antibody-based system. The ordinary artisan at the time the invention was made would have been motivated to test B cells and/or T cells for the presence of TSE using antibodies since this sort of test method utilized a sensitive reagent/ligand, antibodies; to assay cell types that were easily obtainable by non-invasive methods from living animals, in contrast to the other art-recognized approach of brain biopsy. The ordinary artisan at the time the invention was made would have reasonably expected that, as taught by Manuelidis, focusing on a cell type known to be infectious would increase the sensitivity of detection assays, including antibody-based assays. In addition, it was well known in the art at the time the invention was made that once an antibody was developed, the antibody could be used with a reasonable expectation of success to detect an antigen on intact cells, as in a buffy coat of whole blood, by either mounting them on slides for immunohistochemical analysis; or by using other techniques well known in the art at the time the invention was made for intact cell analysis with antibodies. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

20. No claim is allowed.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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September 20, 2001

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